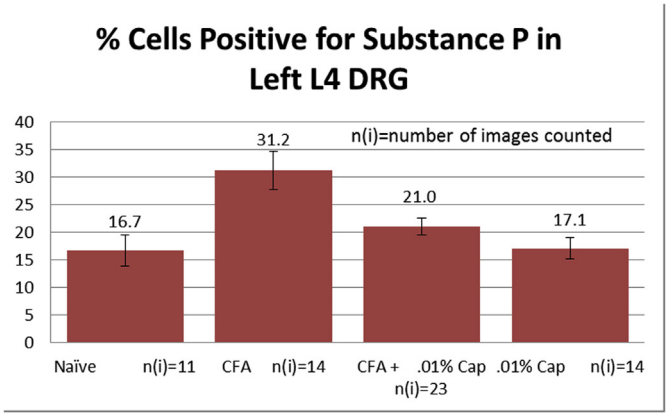
by EPS and ADWB. CAP did not improve ADWB or EPS. These results are different than those found in mice with acute inflammatory arthritis that were pretreated with vanilloids. SP expression in the DRG of arthritic mice was increased compared to naïve but IA treatment with CAP normalized this expression. The use IA RTX or CAP for analgesia in chronic inflammatory arthritis will require additional consideration of optimal dose and timing of administration which has yet to be determined.



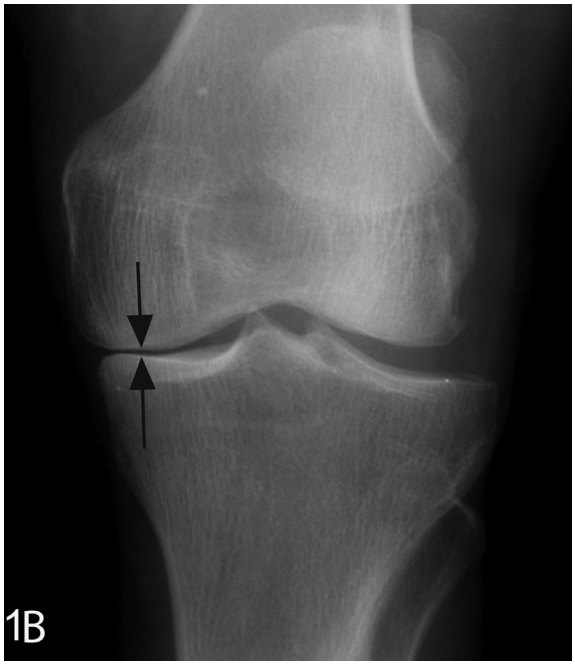




Fig1B. 6 months follow-up radiograph depicts definite medial joint space narrowing (JSN; arrows) with persistent absence of osteophytes medially consistent with RPOA.

**590**

## RELEVANCE OF IMAGING IN ANTI NERVE GROWTH FACTOR INHIBITOR (ANGF) STUDIES WITH A FOCUS ON ELIGIBILITY AND ON-STUDY SAFETY – A PICTORIAL OVERVIEW

F.W. Roemer †, C. Miller ‡, K. Hoover §, C. Hayes ||, C. West ¶, M. Brown ¶, R. Clemmer ¶, A. Guermazi †. † *Boston Univ. Sch. of Med., Boston, MA, USA;* ‡ *BioClinica, Princeton, NJ, USA;* § *Virginia Commonwealth Univ., Richmond, VA, USA;* || *Virginia Commonwealth Univ., Richmond, PA, USA;* ¶ *Pfizer, Groton, CT, USA*

**Purpose:** Monoclonal antibodies that bind and inhibit nerve growth factor (NGF) have demonstrated both good analgesic efficacy and improvement in function in patients with osteoarthritis (OA). Anti-(a) NGF therapies offer potential as the first new class of analgesics for many years. Despite promising efficacy data, trials in OA were suspended due to concerns over accelerated rates of OA progression in some patients. However, continued development of aNGF drugs with rigorous safety screening criteria in future trials is planned and imaging will play a crucial role. Imaging will be used to define the eligibility of potential participants and to monitor safety during the course of these studies in order to identify subjects at risk for rapidly progressive OA (RPOA) prior to inclusion or to withdraw subjects from treatment early due to the occurrence of joint safety events such as RPOA.
The aim of this presentation is to describe and illustrate MRI and radiographic imaging findings that will be important for patient eligibility and safety monitoring in planned studies of aNGF compounds.
**Methods:** This illustrative presentation is based on repetitive meetings of four experienced musculoskeletal radiologists to define potential


Fig 1A. Baseline radiograph shows a normal medial and lateral joint space width.

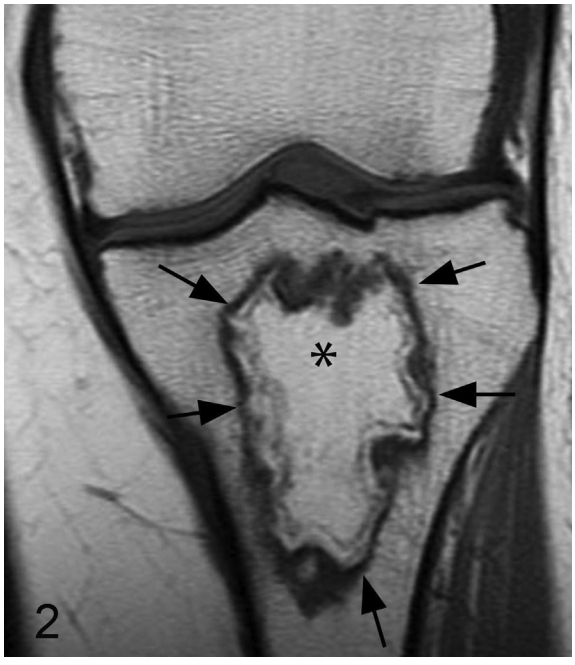



Fig 2. Coronal T1 weighted MR image shows typical metaphyseal osteonecrosis (arrows) with central fat-like signal (asterisk).

eligibility and safety findings relevant for aNGF clinical trials. More than 400 images were reviewed to define the most relevant and characteristic imaging findings.
Diagnoses of exclusion for eligibility due to potentially increased risk of RPOA are subchondral insufficiency fractures (SIF), atrophic OA and severe malalignment of the knee in the medial-lateral direction. Diagnoses relevant for safety after enrolment (i.e. joint safety findings), i.e. RPOA, SIF, osteonecrosis and pathologic fractures will also be discussed. Several of these diagnoses have non-specific findings on the radiograph or cannot be detected radiographically in early stages. Thus, in cases of inconclusive or suspicious radiography, an additional MRI examination may be acquired to rule out or confirm some of these diagnoses.
**Results:** Early and late signs of diagnoses relevant for eligibility will be presented.

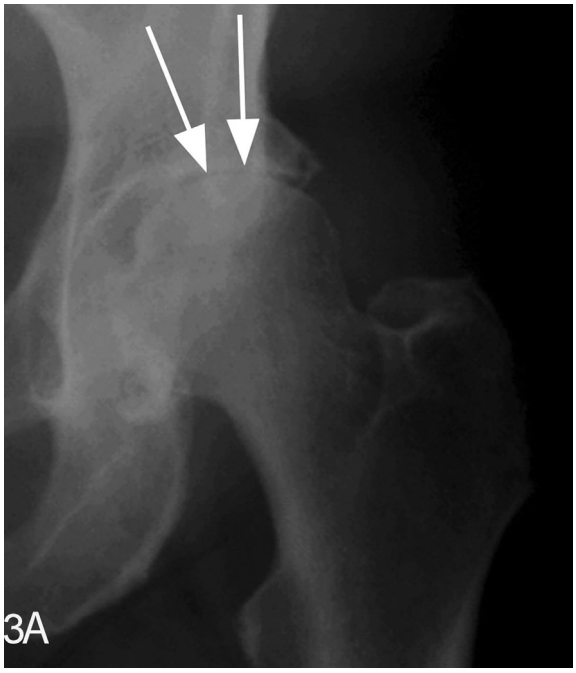



Fig 3A. Radiograph of the hip joint shows superior JSN (arrows) without relevant osteophytes present.

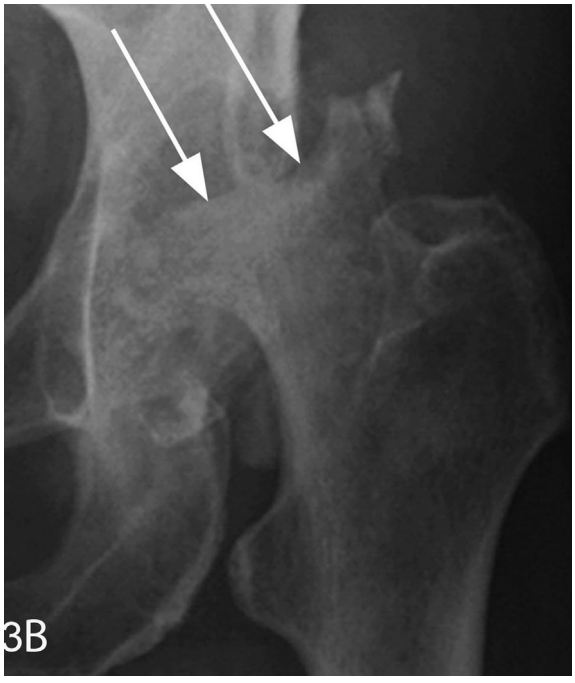



Fig 3B. Follow up image 12 months later shows near-complete destruction of the femoral head (arrows) and subsequent migration of the femur superiorly consistent with RPOA.
**Conclusions:** Expert readers in aNGF programs need to be aware of relevant imaging findings. These include early signs of diagnoses relevant for RPOA on radiography, and other potential X-ray and MRI diagnoses relevant for eligibility and safety during aNGF studies.

## 591
## PROLONGED JOINT RESIDENCY OF TRIAMCINOLONE ACETONIDE AFTER AN INTRA-ARTICULAR INJECTION OF FX006, A SUSTAINED RELEASE FORMULATION FOR THE TREATMENT OF OSTEOARTHRITIS

N. Bodick †, J. Lufkin †, C. Willwerth †, J. Hauben †, A. Kumar †, P. Boen †, J. Bolognese ‡, C. Schoonmaker ‡, M. Clayman †. † *Flexion Therapeutics, Burlington, MA, USA;* ‡ *Cytel Inc, Cambridge, MA, USA*

**Purpose:** Although available intra-articular (IA) corticosteroids are well established in the treatment of painful osteoarthritis (OA), limitations include short duration of pain relief (1-4 weeks), an effect consistent with the transient residency of these compounds in the joint and high plasma corticosteroid concentrations immediately following injection. FX006 is a novel IA sustained-release injectable formulation of 25% triamcinolone acetonide (TCA) in poly(lactic-co-glycolic acid) microspheres intended to prolong therapeutic concentrations of TCA in the joint and limit systemic exposure. In a previously described 6-week long clinical study, FX006 at 40 mg demonstrated maintenance of synovial concentrations of TCA consistent with pharmacologic activity for a period of at least 6 weeks, when levels of TCA produced by an equivalent dose of TCA IR were below the limit of quantitation. The current study extended these data on joint residency by measuring synovial fluid levels of TCA at later time points.
**Methods:** In this multi-center, open-label study, patients with OA of the knee received a single IA injection of FX006 containing 10 or 40 mg TCA, or 40 mg of a standard, immediate-release suspension of TCA (TCA IR). A total of 50 patients were enrolled (FX006 10 mg: 10 patients, FX006 40 mg: 30 patients, TCA IR: 10 patients). Synovial fluid and plasma samples were obtained at baseline (pre-dose) and at the planned Final Visit at either Week 12, 16, or 20, depending on cohort assignment and availability of fluid in the knee. Concentrations of TCA were measured in plasma or in filtered synovial fluid samples using High Performance Liquid Chromatographic methods with Tandem Mass Spectrometry Detection and Automated Extraction, validated for the determination of TCA in human plasma and synovial fluid respectively. The quantitation limits of both assays were 50 to 50000 pg/mL.
**Results:** In the FX006 10 mg group, 8 patients had synovial fluid available for analysis at Week 12. In the FX006 40 mg group, 6 patients had synovial fluid available for analysis at Week 12, 8 patients at Week 16 and 11 patients at Week 20. In the TCA IR group, 5 patients had synovial fluid available for analysis at Week 12. The concentrations of TCA achieved by 40 mg FX006 in the synovial fluid at Week 12 were 924 pg/mL, at Week 16, the IA concentrations of TCA were 224 pg/mL and by Week 20 they were below the lower limit of quantitation (Figure; geometric means from the earlier 6-week study and the current study are merged). The IA concentration of TCA in patients receiving 40 mg of TCA IR at Week 12 was below the lower limit of quantitation. FX006 maintained a gradient between synovial and systemic plasma concentrations of TCA for 16 weeks.